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HISTOPATHOLOGICAL STUDY OF MENINGIOMAS IN RELATION TO IMMUNOHISTOCHEMISTRY MARKER- PR

Pathology

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ABSTRACT

Meningiomas are slow growing, dural based central nervous system tumors. Increased growth in pregnancy, high prevalence in females, suggests a female hormonal role. Anti-hormonal therapy is suggested in such patients.

AIM: To study and evaluate PR status in various types of meningiomas.

MATERIALS AND METHODS: This is a retrospective study undertaken at Department of Pathology ESIC-SSH Sanathnagar, Hyderabad, Telangana,India, from January 2017 to December 2019.The biopsies which were received at the Department of Pathology, ESIC-SSH and diagnosed as Meningiomas on histopathology were studied in correlation with the PR status.

RESULTS: Out of the total of 70 cases, we had 44 females and 26 males. The predominant age of presentation is in the age group of 41-50 years. Meningotheliomatous meningioma is the commonest one. PR positivity is more in Grade I tumors and female patients.

CONCLUSION: Thus, meningiomas show higher PR positivity indicating that PR plays a pivotal role in the pathogenesis and molecular biology of these tumors.

KEYWORDS

Meningioma,Immunohistochemistry,Progesterone Receptor.

INTRODUCTION:

Meningiomas are the most common dural based tumors of the nervous system [1,2]. They can occur both in intracranial and in spinal locations. Meningiomas are neoplasm with distinct biological attributes. They grow slowly and rarely infiltrate the brain.

They account for 15-30% of all primary intracranial tumors and 25% of intraspinal tumors. They are thought to arise from the meningothelial cells of the arachanoid villi of the meninges. The word Meningioma was coined by Harvey Cushing[3].

Meningiomas are more common in females than males with F: M ratio of incidence around 8:1. These tumors grow in pregnancy and luteal phase of menstruation. This is attributed to the influence of the PR receptors detected in most of the meningiomas. Some studies also point towards the data that meningiomas tend to occur more in patients with breast cancer[4].

With a vast research data pointing out the role of PR receptors in the growth and prognosis of meningiomas, our present study aims at the histopathological correlation of these tumors with the PR status.

MATERIALS AND METHODS:

This study is a retrospective study undertaken at Department of Pathology ESIC-SSH Sanathnagar from January 2017 to December 2019. The biopsies which were received at the Department of Pathology,ESIC-SSH and diagnosed as Meningiomas on histopathology were studied in correlation with the PR status.

For all the cases the specimens were fixed in 10% neutral buffered formalin. If the tumor was submitted in fragmented bits all the tissue was processed. If the tumor was sent as a whole, 0.5 cm slices were taken and representative sections were given. The tissue bits were processed and embedded in wax.

The paraffin embedded blocks were cut at 3- 4 micron thickness. Sections stained and routine haematoxylin and eosin stain was used. Subtyping and grading was done according to WHO classification and grading system.

Immunohistochemical staining was performed on 3-4 micron thick sections.The sections were taken on a polylysine pre coated slides. Method which is used involves a secondary antibody conjugated to PolyHRP reagent which binds to primary antibody. This complex is visualised by DAB chromogen. Microwave is the method used for antigen retreival.

Negative controls and positive controls were used. Negative controls wherein the secondary antibody is skipped. The positive control being breast cancer which is PR positive.

RESULTS

Table I: Gender Distribution Of Three Grades Of Meningioma

Gender	GradeI	GradeII	GradeIII	TOTAL
Male	24	2	-	26
Female	36	6	2	44

Out of the total of 70 cases, we had 44 females and 26 males making the M:F ratio to 1.7:1 with a female preponderance.

In 26 male, 24 patients showed Grade I, 2 patient showed grade II tumor. In 44 female, 36 patient showed Grade I, 6 patients showed Grade II tumors, 2 patients showed WHO Grade III tumors. Thus, both in the male and females Grade I tumors are more common than Grade III tumors.

Table II: Age Wise Distribution Of Three Grades Of Meningioma

AGE	Grade I	Grade II	Grade III	TOTAL
20-30	2	_	_	2(2.8%)
31-40	8	2	_	10(14.2%)
41-50	24	2	2	28(40%)
51-60	14	4	_	18(5.7%)
61-70	10	_	_	10(14.2%)
71-80	2	_	_	2(2.8%)
TOTAL	60	8	2	70

Meningiomas are primarily tumors of middle age. The youngest patient in our study is 30 year old and the eldest age of presentation is 71 year old. The mean age of presentation is 50.5 years. There are about 28 patients in the age group of 41-50 years age group. The second most common age group is 51-60 years .In our study even in the older age group Grade I tumors are more common. Grade III and grade II tumors were more common in the 41-50 years age group. Thus meningiomas were less in the extremes of age, 2cases in 20-30 age group and 2 cases

in 71-80 age group.

Table III: Site Wise Distribution Of Three Grades Of Meningioma

SITE	Grade I	Grade II	Grade III	TOTAL
Temporal	8	_	_	8(11.4%)
Parietal	20	4	2	26(37.1%)
Sphenoidal	4	_	_	4(5.7%)
Frontal	16	2	_	18(25.7%)
cerebellum	2	_	_	2(2.8%)
Spinal cord	2	_	_	2(2.8%)
Parafalcine	2	_	_	2(2.8%)
Cavernous sinus	2	_	_	2(2.8%)
Lateral ventricle	2	_	_	2(2.8%)
Occipital	2	-	-	2(2.8%)
Cerebellopontine angle	_	2	_	2(2.8%)
TOTAL	60	8	2	70

Cranial meningiomas are more common when compared to spinal meningiomas.

Out of the various locations, parietal lobe is the commonest site followed by frontal lobe. Thus, meningiomas are more common in the supratentorial location. They are rare in the cerebellum and spinal cord. In the spinal cord both the tumors were in the thoracic region. There was no site predilection for higher grade tumors in the present study. The Grade III tumors also occurred in parietal lobe.

Table IV: Histological Variants Of Meningiomas

Histological type	PR Positive	PR Negative	TOTAL
Meningothelial meningioma	38	18	56(80%)
Angiomatous meningioma	-	2	2(2.85%)
Fibrous meningioma	2	-	2(2.85%)
Atypical meningioma	8	-	8(1.4%)
Malignant meningioma	2	-	2(2.85%)
TOTAL	50	20	70

Out of the 70 meningioma cases, 56 cases are meningothelial meningiomas, 2 angiomatous meningioma, 2 fibrous meningioma, 8 atypical meningioma, and 2 malignant meningioma (Figure I, II, III, IV, V and VI) respectively. This forms 60 cases of Grade I tumors, 8 cases of Grade II tumors and 2 cases of Grade III tumors.

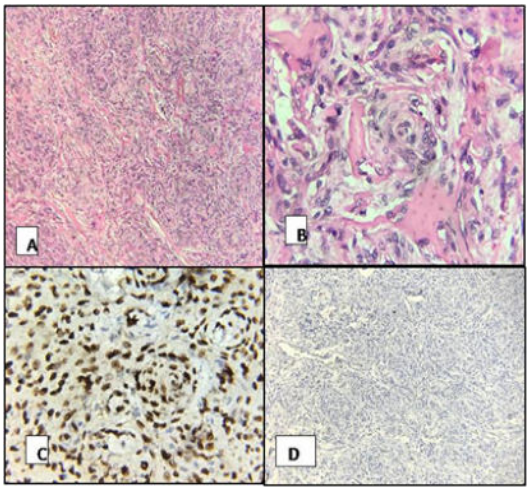

Figure I: Meningotheliomatous Meningioma (A) H&E 10x (B) H&E 40x (C) Immunohistochemistry PR Positive (D) Immunohistochemistry PR Negative

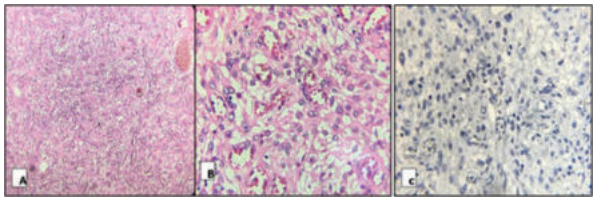

Figure II: Angiomatous Meningioma (A) H&E 40x (B) H&E 10x (C) Immunohistochemistry -PR Negative.

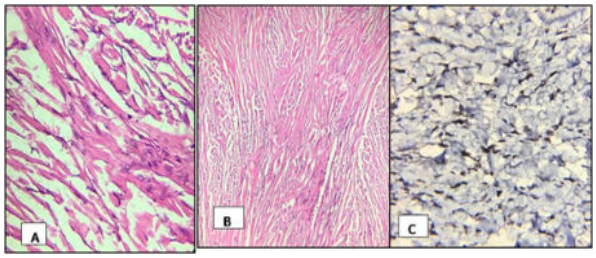

Figure III: Fibrous Meningioma A}H&E 40x B}H&E 10x (C) Immunohistochemistry PR Positive

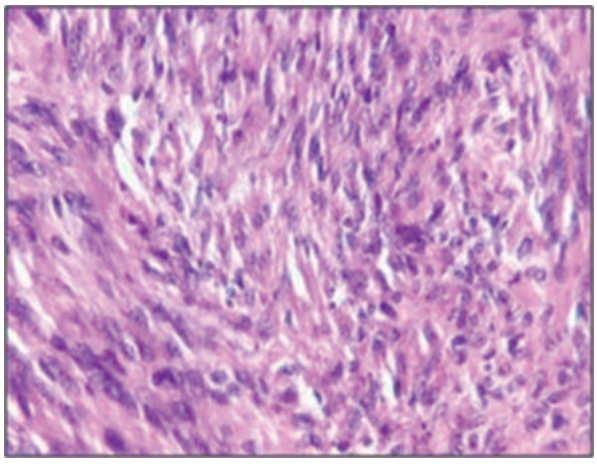

Figure IV: Atypical Meningioma. H&E 40x

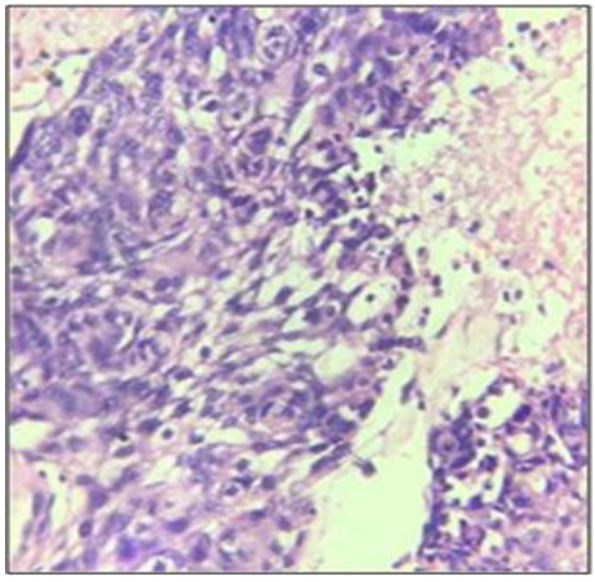

Figure V: Malignant meningioma with areas of necrosis. H&E 40x

Table V: PR Positivity In The Three Grades Of Meningiomas

Grade	PR positive	PR negative	TOTAL
I	40	20	60(85.6%)
II	8	-	8(11.4%)
III	2	-	2(2.85%)
TOTAL	50	20	70

Out of the 70 cases of meningiomas, 50 cases are PR positive and 20 cases are PR negative. In the meningothelial meningioma 38 are PR positive and 18 are PR negative. Both the cases of angiomatous meningioma are PR negative. The cases of fibrous meningioma, atypical and malignant meningioma are all PR positive. This results in most of the Grade I (85.5%), all of the Grade II and Grade III meningiomas being PR positive.

PR Positivity in relation to gender: PR positivity did not show any sex predilection in the present study. The PR status was positive in 36 cases

of the 44 female (80%) and 14 cases out of 26 male cases (53.8%). The PR positive status was more in females than in males. However PR receptor positivity was also seen in males.

Table VI: Gender Wise PR Positivity

GENDER	PR positive	PR negative	TOTAL
FEMALE	36	8	44(62.8%)
MALE	14	12	26(37.14%)
TOTAL	50	20	70

DISCUSSION

Meningiomas are meningothelial cell neoplasm attached to the inner surface of the duramater. Meningiomas can occur along any of the external surface of the brain, spinal cord as well as within the ventricular system. Meningiomas mostly occur in the middle age and elderly patients. In the middle age, the tumors mostly occur in the females. Atypical and anaplastic meningiomas occur more in the males[1]. They are classified into WHO Grade I, Grade II and Grade III depending on their prognostic and biological behavior.

Meningiomas account for 25%-30% of primary intracranial tumors. Atypical meningiomas constitute 20% of meningiomas. Anaplastic meningiomas account for 1.5% of meningiomas. In the past few years the relationship between meningiomas and the female sex predilection, have paved way to the studies on hormonal receptor analysis. Among the hormonal receptors, PR receptor studies were studied in the forefront.In this present study we present the statistical analysis of meningiomas, their hormonal receptor analysis, their age and sex distribution etc. In the present study, out of the 70 cases of meningiomas, 44 cases were in females and 26 cases were in males. The M: F ratio being nearly 2:1, thus, showing female preponderance. This is in concordance with many studies like Roser F, Sanghamitra mukherjee, Ramesh babu telugu. These results are not in concordance with studies of Gursan and studies like Srilakshmi.

Similarly, the mean age of presentation of the tumors was 50.5 years; this was in concordance with Ramesh babu, Srilakshmi. The maximum number of cases presented was in the age group of 41-50 years of age.

Out of the 70 cases evaluated, 56 cases (80%) are meningothelial meningiomas, 2 angiomatous meningiomas, 2 fibrous meningiomas, 8 atypical meningiomas and 2 malignant meningiomas. This forms 60 cases of Grade I tumors, 8 cases of Grade II tumors and 2 cases of Grade III tumors. This was different from studies like Mukherjee,Gursan and Srilakshmi who inspite of showing meningotheliomatous meningioma to be the predominant type, had higher percentage of fibrous meningiomas, transitional meningiomas and psammomatous meningiomas.

In the present study the intracranial meningiomas are the predominant site than the spinal meningiomas. In the brain parietal convexity was the predominant site of involvement with 37.1% of cases in parietal convexity followed by frontal meningiomas with 25.7%. This was in concordance with studies like Yusriany R[5] and Srilakshmi[3] who had cerebral convexity occurrence in 29.4% cases and 37.27% respectively.

We have found PR positivity in 50 cases (71.2%) which were in concordance with studies like Gursan, Nagashima which also showed positivity in 72% of cases[6,7].

In our study female (62%) had greater PR positivity than male (37%). This was in concordance with Ramesh Babu telugu and Mukherjee[8,2], which showed 75% and 83% respectively.

In our study PR expression was more in meningothelial variant, angiomatous, atypical and malignant meningioma. These data was conflicting with many studies like Roser, Mukherjee which showed negative PR in anaplastic and atypical variants. However, higher PR positivity in meningotheliomatous variant was in accordance with Roser and Mukherjee[4,2].

Thus, meningiomas are a diverse group of mostly benign tumors with a distinct biological behavior.

CONCLUSION

Thus, meningiomas are the most common benign neoplasms of the cranium[9]. These tumors are more common in the supratentorium. They are more common in females with age predilection to 41-50 years age group. Meningotheliomatous meningiomas are the most common variety in the present study. PR positivity is more in the Grade I tumors and in females[10]. The occurrence, site, sex and age predilection is similar with other parts of the world.

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